

Translated from the Russian

Tel'tsa Provacheka pri Trakhome i Ikh Epidemiologicheskoe Znachenie

Prowazek Bodies in Trachoma and Their Epidemiological Significance

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THE DISCOVERY of bacterial carriage, the elucidation of the role of the human carrier in the spread of contagious diseases, and the development of epidemics are of exceptionally great importance.

At the present time, the carrier state has been studied and established for many diseases, for example, typhoid fever, bacterial dysentery, cholera, diphtheria, scarlet fever, plague, tularemia, brucellosis, pertussis, epidemic hepatitis (Botkin's disease), poliomyelitis, syphilis, tuberculosis, and in a number of ultravirus (N. F. Gamaleya), protozoan (various types of malaria), and other infectious diseases (I. R. Drobinskiy, 1953).

Trachoma has long been recognized as an infectious disease, and recent investigations have almost completely confirmed the virus origin of

it. The elementary bodies of the Prowazek-Halberstaedter intracellular inclusions are considered to be the only causal agents of trachoma (V. V. Chirkovskiy, M. P. Chumakov, Sh. D. Moshkovskiy, A. A. Avakyan, N. A. Zaytseva, A. L. Kankrov, P. N. Zhurin, Grosfel'd, P. Thygeson, Ishihara, and others).

We have set before ourselves the task of clarifying, by means of conjunctival scrapings for Prowazek-Halberstaedter bodies, the question of whether a carrier state exists in clinically healthy persons in foci of trachoma and in those who are clinically cured convalescents, that is, in stage 4 of trachoma.

In the literature available to us we have not been able to find much information concerning the detection of Prowazek bodies in the clinically normal ocular mucosa.

A. L. Kankrov (1928), who was a proponent of the specific nature of the intracellular inclusions in trachoma, noted the presence of trachomatous inclusions in the conjunctiva under certain conditions even in the absence of the clinical picture of trachoma. He observed that "when trachoma was present in one eye, intracellular inclusions were found in the scrapings of the other, healthy eye." "Could it be certified," he asked, "that their presence there is not the beginning of the disease, which has not yet manifested itself in any way?" (quoted by V. V. Chirkovskiy, *Vestnik Oftalmologii*, 1950, No. 3).

In her work (at the Trachoma Institute at Ashkhabad, devoted to the specificity of the Prowazek bodies in trachoma) Gorbunova pointed out that acute epidemic conjunctivitis produced by the Koch-Weeks, Morax-Axenfeld bacilli, and others were accompanied

in 13.7 percent of the cases by the appearance of the intracellular inclusions of Prowazek (quoted by V. V. Chirkovskiy, *Vestnik Oftalmologii*, 1950, No. 3). However, she did not report whether or not the clinical picture of trachoma developed after the conjunctivitis were cured. If not, then it is possible that in the given cases virus carriage existed, and the conjunctivitis exerted a provocative influence on the appearance of the Prowazek bodies.

Izabolinskiy and V. I. Spasskiy also speak of the presence of Prowazek bodies in the normal conjunctiva.

P. N. Zhurin (1951) examined 51 healthy eyes in 43 persons; of these, 27 persons had trachoma in only 1 eye. Prowazek bodies were found in conjunctival scrapings of five healthy eyes in five persons who had a disease in the other eye suspected of being trachoma, and in which Prowazek bodies were present.

The day after the Prowazek bodies were found, the healthy eyes became diseased in all cases, and after 2 days, a clinical, acute conjunctivitis developed, followed later by typical trachoma in both eyes. The author believes that the Prowazek bodies were found by him in the last few days of incubation, although this contradicts the data of Miyashita, who after an artificial transplantation of trachoma from person to person did not find Prowazek bodies in the incubation period.

Of the foreign authors, Bodian (1947) reported that out of 100 Fiji natives working for the American Army, signs of trachoma were found in 22 clinically. In 15 of these 22 persons, typical Prowazek bodies were found in the epithelial cells. Of 78 persons who did not have clinical signs of trachoma, 27 had inclusions morphologically identical with the inclusions found in the trachoma patients. Transmissibility and pathogenicity of the trachoma virus in these persons were not proved by the author, nor were the results of further observation of them described.

It is known that Prowazek inclusions are found most often in fresh trachoma or even in the prefollicular stage (Grosfel'd, G. Kh. Kudoyarov, and others) as well as in untreated trachoma. After treatment, they disappear or are found with great difficulty, and after therapy is stopped they can be demonstrated again.

In cicatricial trachoma they are very rarely found (V. P. Odintsov).

At the suggestion of V. V. Chirkovskiy (1953), trachoma in which the cicatrization of the conjunctiva has been completed, with no hyperemia or infiltration, is distinguished as stage 4 (absolute trachoma).

"Separation of the fourth period of trachoma into a special clinical form," writes V. V. Chirkovskiy, "is expedient for the purpose of characterizing the conclusion of the process, although, in essence, it is the same, third period of trachoma, the cicatricial. Establishment of its presence is important also in an epidemiological connection, because this period, in contrast to the others, is considered noninfectious by us."

Later, he mentions "that by the fourth period we understand not only those resultant forms of trachomatous inflammation where there is diffuse terminal cicatrization of the lids but also those cases where the trachoma has been concluded with the formation of individual scars, even though hardly noticeable, but where the conjunctiva does not show inflammatory signs."

According to the data of A. L. Kankrov (1928), in cicatricial trachoma (it must be assumed that this is the fourth stage, according to the modern classification) Prowazek bodies are rarely found.

In the literature available to us in recent years we have not been able to find any reports of investigations of Prowazek bodies in the fourth stage of trachoma.

In his work at the Chuvash Trachoma Institute, 1951, devoted to the problem of Prowazek bodies, P. N. Zhurin examined 1,039 trachoma patients admitted for the first time and in stages 1, 2, and 3, but apparently no investigations were carried out for Prowazek bodies in stage 4 trachoma patients.

From November 1952 through December 1954 the Izhevsk Medical Institute eye disease clinic examined 11 inhabited places with the aim of demonstrating Prowazek bodies both in trachoma patients and in clinically healthy persons. Trachoma patients in each of the four stages, persons suspected of trachoma, those with follicular and catarrhal conjunctivitis, as well as persons with clinically healthy palpebral conjunctivae were included.

For each inhabited place a special examination journal was kept on the type of the family-homestead list card. Each journal sheet was designed for a single family.

In order to obtain a surface scraping of the conjunctiva, the upper lid of the eye under examination was everted on a lid elevator, and in cases where the conjunctiva was contracted, even without the aid of the lid elevator, a conjunctival scraping was taken with a dull scalpel from the area of the upper edge of the cartilage and the plica semilunaris (superior fornix). In certain cases, depending on the picture of involvement of the conjunctiva, the scrapings were taken from the plica semilunaris of the lower lid [inferior fornix]. The material obtained was spread out on a glass slide. From the material taken from each eye a single preparation was made. The scrapings were examined in the clinic laboratory. They were stained by the Romanowsky-Giemsa method, without fixation.

We classified the Prowazek bodies in groups as typical or atypical. Bodies with definite granulation in the form of caps around the nucleus of the epithelial cell belonged to the typical group. With respect to number, the bodies detected were classified as multiple, when there were two to three or more bodies in the microscopic field or in the preparation (in three patients with stage 4 trachoma there were three to four bodies in the microscopic field), and single, when after prolonged search only one or two Prowazek bodies were found in the preparation.

Prowazek bodies were considered atypical in which the granulation existed in the form of compact granular clumps disposed near the nucleus of the cell, or in cases of those bodies which were found in a stage of lysis.

P. N. Zhurin believes that "at the present time all the so-called atypical inclusions cannot be regarded as nonspecific substances, and one cannot avoid studying them and taking them into consideration in the evaluation of the problem of the etiological role of Prowazek inclusions."

We examined scrapings for Prowazek-Halberstaedter bodies in 2,933 persons. Of these, there were 53 persons suspected of trachoma, 13 with stage 1 trachoma, 19 with stage 2

trachoma, 491 with stage 3 trachoma, and 795 with stage 4 trachoma, 151 with catarrhal conjunctivitis, subacute and chronic, and 114 with follicular conjunctivitis. There were 1,297 clinically healthy persons.

On examination of the scrapings, Prowazek bodies were found in 3.8 percent of the persons suspected of trachoma. In patients who had trachoma they were found as follows: stage 1, in 23 percent; stage 2, 10.5 percent; stage 3, 9.49 percent; and stage 4, 4 percent. They were found in 0.7 percent of patients with catarrhal conjunctivitis, in 1.8 percent with follicular conjunctivitis, and in 1 percent of clinically healthy persons.

If account is also taken of the atypical Prowazek bodies found, the percentage of positive results is increased in all patients with the exception of the persons suspected of having trachoma and patients with stage 1 trachoma. The percentage of atypical bodies compared with typical ones was particularly high in clinically healthy persons: typical, 1 percent; atypical, 1.85 percent; together, 2.9 percent.

Of the 795 patients with stage 4 trachoma, 249 had been spontaneously cured, 271 had been treated in early childhood, 158 had been treated at intervals, and 117 had received systematic treatment.

Of the group of patients with stage 4 trachoma, antirelapse treatment had been conducted in only 168; of these, typical Prowazek bodies were found in 4 persons (2.4 percent). Of the 627 patients who had not received antirelapse treatment, there were more with typical Prowazek bodies, 4.55 percent. In the great majority of patients single Prowazek bodies were found, including those who had had a spontaneous cure, those treated in early childhood, those treated at intervals, and those treated systematically.

As had already been mentioned, of the 1,297 clinically healthy persons typical Prowazek bodies were found in 13 (1 percent); atypical ones, in 24 (1.8 percent). We wanted to clarify whether or not there was a difference in the percentage of Prowazek bodies found in contacts and in those who had not had contact with the disease. There was practically no difference—2.5 and 3.2 percent, respectively.

Data of an ordinary clinical examination with

the naked eye, or sometimes with the aid of a binocular magnifying glass, make it possible to decide that the trachomatous process had been concluded; nevertheless, as has now been established, foci of still-smoldering infection are found in a significant portion of the cases when they are examined by means of a slit lamp (N. Ya. Pokhisov, K. I. Golubeva, T. I. Voinova, T. D. Zatsepina, and others).

In order to clarify whether a state of cure of the trachomatous process existed, we (F. F. Sysoyev, N. T. Novoselova) checked 73 patients with stage 4 trachoma who were under the observation of the polyclinic group of the eye clinic. Examination was made of the conjunctiva and cornea by means of the slit lamp, and scrapings were taken for Prowazek bodies. In one of this group of patients the diagnosis of stage 4 trachoma was not confirmed by the slit lamp examination. No changes were found in the conjunctiva or cornea. He was healthy. No Prowazek bodies were found on two examinations of scrapings. There was no one who had trachoma in the family. In the other 72 patients, slit lamp examinations and examinations of scrapings were conducted once in 38, twice in 25, 3 times in 8, and 4 times in 1 patient.

In 30 trachoma patients complete cure had not occurred, and pathological elements were found in the form of small focal infiltrations and solitary follicles deeply situated in the tarsal conjunctiva. Of the patients in this group, Prowazek bodies were found in two. Often, cases were noted where the trachomatous process proved to be terminated in the conjunctiva of the lower lids, while there were elements of unhealed trachoma on the conjunctiva of the upper lids.

On repeated examinations of 30 patients with stage 3 trachoma no particular changes were noted in the clinical picture: the focal infiltration did not decrease, and the deep-seated follicles were not absorbed (6 months of observation). Stage 3 trachoma passed into stage 4 trachoma in only 1 patient.

Of 42 patients examined by the method of biomicroscopy, Prowazek bodies were found in 1.

Regressive or cicatricial pannuses of varying degrees of activity were found in all patients on examination with the slit lamp.

As has already been mentioned, out of the 2,933 persons, stage 4 trachoma was established in 795 by an ordinary examination, and Prowazek bodies were found in 45 of the 795 persons. Forty-three patients in whom there were Prowazek bodies were checked by the slit lamp at various periods after the first examination (6 to 24 months); of these, the trachoma remained unhealed in 19. Just as in the preceding group, small focal infiltration and solitary, deeply seated follicles were found in the tarsal conjunctiva (stage 3). Of the patients in this group, Prowazek bodies were found repeatedly in five.

Twenty-two persons proved by slit lamp examinations to be cured. Prowazek bodies were found repeatedly in two persons; two others had no signs of having had trachoma (healthy).

Therefore, of 116 patients in whom stage 4 trachoma had been established by the usual methods of examination, unhealed trachoma was found in 49 with the aid of the slit lamp; Prowazek bodies were found both in the unhealed and in the healed (convalescent carriage) cases.

Thirty-six persons who were clinically healthy but had Prowazek bodies were checked with the slit lamp; 17 proved to be completely healthy, 13 had stage 4 microtrachoma [very small trachomatous area], and there was 1 patient each with stage 4 trachoma, with follicular conjunctivitis, with folliculosis, with stage 3 microtrachoma, and with stage 3 trachoma. One was not accounted for.

Prowazek bodies were found repeatedly in two of the group of biomicroscopically healthy persons.

Two persons were checked for follicular conjunctivitis: in one a follicular conjunctivitis was shown; in the other, a *forme fruste* of trachoma. Of two patients with chronic conjunctivitis both proved to be healthy [with respect to trachoma]; in those with acute conjunctivitis, one proved to be healthy. In these patients it was impossible to find Prowazek bodies in repeated scrapings.

As has been mentioned, typical Prowazek bodies were found in 13 clinically healthy persons. On slit lamp examination, six persons of this group were shown to have healthy conjunctivae, while Prowazek bodies were found re-

peatedly in one. In one of those examined, typical Prowazek bodies were found repeatedly, whereas at first examination, atypical Prowazek bodies had been found. We found atypical Prowazek bodies in clinically healthy conjunctiva, as well as in stage 2, 3, and 4 trachoma, which confirms P. N. Zhurin's opinion that "at the present time all the so-called atypical inclusions cannot be regarded as nonspecific substances, and one cannot avoid studying them and taking them into consideration in the evaluation of the problem of the etiological role of Prowazek inclusions."

Therefore, it may be considered that Prowazek bodies are found in biomicroscopically established stage 4 trachoma (convalescent carriage) as well as in clinically healthy persons (virus carriage).

Those cases of carriage among persons clinically completely healthy in foci of trachoma, where it was also possible for us to establish trachoma biomicroscopically, are in accordance with the concept of carriage as it applies to other diseases.

Perhaps, at the current stage of our knowledge it is impossible to exclude the existence of asymptomatic trachoma in cases where the clinical manifestations of trachoma cannot be established by our methods, even by the slit lamp, even though Prowazek bodies are found.

For practical purposes it is very important to establish the criteria of recovery in trachoma. Apparently, even the slit lamp examination does not give complete assurance of the termination of the process. In certain cases with apparent clinical recovery histological examination reveals infiltration in the depth of the tissue (V. V. Chirkovskiy, V. N. Spasskiy, N. M. Pavlov, K. I. Golubeva, and others).

Absence of Prowazek bodies in clinically terminated trachoma is not always conclusive proof of complete healing, because Prowazek bodies are not always easily found even in cases where they may be present. Their presence in clinically healed trachoma undoubtedly speaks for the incomplete elimination of the trachoma virus from the conjunctiva (convalescent carriage), because "clinical recovery (temporary or permanent) is far from being always associated with the elimination of the pathogenic

causal organisms from the body" (I. R. Drobin-skiy, 1953).

It may be supposed that with clinical healing of the trachomatous process (stage 4) in certain cases the virus is kept in a latent condition without producing any reactions in the ocular mucosa for a long time. However, sometimes, apparently through the influence of factors of the internal milieu and under the effect of external causes, the virus can become activated and multiply; this is manifested clinically by what we call a relapse.

G. Kh. Kudoyarov mentions the *forme fruste* of trachoma; N. M. Pavlov, the latent form; M. I. Averbakh, N. Ya. Pokhisov, and others, microtrachoma. In prophylactic examinations carried out on a large scale such patients are recorded as clinically healthy, and it is not taken into consideration that they are virus carriers. Under certain conditions, given the presence of the trachoma virus and under the influence of factors of the internal or external milieu, the characteristic clinical picture of the disease can develop, diagnosable by ordinary methods of examination. How else can those cases of trachoma be explained where no source of infection is established?

Everything which has been said is of tremendous epidemiological significance and makes it necessary to observe and conduct prophylactic measures systematically in foci of trachoma even in the event all the members of a family are considered cured.

As far as fresh cases are concerned, which in practice are recorded as "new infections," they apparently are not always new; in certain cases, the so-called latent cases or the *formes frustes* of trachoma during exacerbations can give the picture of stage 1 trachoma (G. Kh. Kudoyarov). The possibility of serious relapses in stage 4 microtrachoma has not been excluded either.

Often, complete healing is observed without notable traces on the conjunctiva and cornea revealed by the naked-eye examination both after advanced and incipient forms of trachoma (G. Kh. Kudoyarov). In Udmurt, such cases are recorded, after repeated prophylactic examinations, as stage 4 trachoma ("healthy") in contrast to those cases in which scars are detected by simple examination and which are

recorded simply as stage 4 trachoma. This makes it possible, when a suitable account is kept (yearly records in general examination journals), to evaluate relapses more accurately in case they occur in persons in whom healing has occurred without notable traces, instead of having to record them as a new disease.

Many ophthalmologists believe that there are no relapses in the healed form of trachoma, and if a relapse has occurred it means that the trachoma was not healed, or that a second infection has been sustained. The percentage of relapses among those clinically healed, according to various authors, ranges from 7 to 25 (M. P. Chumakov).

In Udmurt, the percentage of relapses in various rayons [districts], according to the data of the trachoma dispensary, ranges from 1.8 to 12.5, while the average percentage amounts to 8.3.

It should be taken into consideration that the tremendous majority of relapses represent insufficiently healed trachoma. The criteria of cure have not as yet been established. In the large-scale prophylactic examinations the diagnosis is made with the naked eye or at best by means of the binocular magnifying glass, whereby subjectivism is possible.

According to directive No. 43 of the U.S.S.R. Ministry of Health, dated January 16, 1952, patients may be removed from the trachoma record only after their clinical recovery has been established by a medical board, which must draw up a document concerning the state of cure or fill in a special card as a record of the results of antibiotic treatment (A. S. Savvaitov). This directive eliminates subjectivism to a considerable degree and contributes to a more serious approach to the establishment of the state of cure. However, there are relapses even after such conclusions.

The Ministry of Health recommends that observations be made of those who have been removed from the record (stage 4 trachoma) for another 4 to 6 months (A. S. Savvaitov). From the experience of the Udmurt Republic it may be stated that this period of observation is not always sufficient. Relapses may occur sometimes even many years after recovery. Therefore, in foci of trachoma it is not practical to establish periods of observation of those who

have been cured, but rather a systematic observation of them should be conducted without setting time limits.

In rural localities of Udmurt we recommend the checking of all those cured (stage 4) by qualified nurses and feldshers, with whom they register no less than twice a month. In the event signs of a relapse are found, treatment should be begun without waiting for the instructions of the physician, and when the physician visits this inhabited place such patients should be presented for consultation.

Timely detection of relapses and elimination of them is a problem of current importance on a par with treatment of patients who are still active in foci of trachoma. "Outbreaks of fire should be extinguished quickly."

In Udmurt, a large number of patients have been cured in the past 5 years. In certain inhabited places there have been only single patients, whereas there are 50 to 100 or more cured.

Naturally, the problem may arise as to whether it is practical to leave trachoma stations in such settlements, or whether it is time to eliminate them. At the given stage of our knowledge, this is impractical and premature, because the lack of complete clarity in the diagnosis of healed trachoma and the existence of relapses require the unflagging attention to and observation of those in whom the disease has passed into stage 4. If attention to stage 4 trachoma patients is lessened, a new rise in the morbidity rate curve is possible in the foci in consequence of relapses and new infections. Therefore, trachoma stations had to be left in settlements where few active patients remained. However, at such stations there may prove to be insufficient work for the nurses. With what should they occupy themselves, aside from treating patients with trachoma and prophylactic work? Nurses who have not completed their secondary-school medical education should increase their medical qualifications by means of correspondence courses given by the medical schools, while those who have completed secondary medical schools should have their medical qualifications increased by means of seminars organized for them. After their qualifications are increased, the trachoma stations should be converted into kolkhoz medical stations, at

which not only treatment of the trachoma patients remaining and prophylactic work will be carried out, but where also kolkhozniks will receive other forms of medical aid within the limits of competency of the nurse. Thus, gradually, with the elimination of trachoma, the trachoma stations should be reorganized as kolkhoz medical stations.

Conclusions

1. After establishment of the existence of stage 4 trachoma by ordinary methods of investigation, elements of unhealed trachoma remain in almost half of the patients in the form of small focal infiltrations and solitary follicles deeply situated in the tarsal conjunctiva or at the corners of the cartilages (stage 3).

2. Prowazek bodies are found even in those in whom the diagnosis of healed trachoma had been established biomicroscopically (convalescent carriage), which is of epidemiological significance.

3. In foci of trachoma the possibility of carriage of it by persons who are clinically completely healthy has not been excluded.

4. Patients with the so-called *forme fruste* of trachoma, latent trachoma, and microtrachoma are often recorded as healthy in ordinary examinations, but in practice are virus carriers. Therefore, the possibility of infection from them has not been excluded. Under certain conditions, the characteristic clinical picture of the disease can develop in them, diagnosable even by ordinary methods of examinations.

5. The criterion of the state of cure of trachoma, that is of complete safety for those around with a guarantee against relapses, has not as yet been established. Therefore, at the current stage of the fight against trachoma, registration and account of the healed cases (stage 4) and constant observation of them are obligatory, and antirelapse therapy is desirable.

6. The period of 4 to 6 months established for observation of the healed cases (stage 4) should be considered arbitrary. Systematic observation of them should be carried out without definition of periods of time.

7. In view of the relapses observed in those who have been cured, the trachoma (medical) stations in the trachoma foci should be maintained for a certain time even in the event all the patients are cured.

Grants for Evaluating Glaucoma Diagnosis Techniques

A 5-year study to evaluate methods for screening and diagnosing glaucoma in the United States has been launched with the financial support of the Public Health Service's National Institutes of Health.

Techniques currently applied to the detection and identification of glaucoma are now being evaluated at four research centers in this country through grants awarded by the National Institute of Neurological Diseases and Blindness. The grants are expected to total approximately \$115,000 a year.

The grantees are the Wilmer Institute, Johns Hopkins University Hospital, Baltimore; Moffitt Eye Hospital, University of California Medical School, San Francisco; Department of Ophthalmology, Washington University School of Medicine, St. Louis; and the Department of Ophthalmology, State University of Iowa, Iowa City.

The cause of the disease is unknown. Early detection might allow saving the patient's eyesight, but diagnosis in early stages is difficult because the patient often feels no discomfort. Since glaucoma appears to be a family disease, a large proportion of individuals studied will be children of glaucoma patients.

A statistical analysis of the study data is planned by the Chronic Disease Branch of the Service's Bureau of State Services.